Osteoarthritis and Cartilage 27 (2019) 871–877

Osteoarthritis and Cartilage

Opioid use in knee or hip osteoarthritis: a region-wide population-based cohort study

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ARTICLE INFO

Article history:
Received 7 June 2018
Accepted 8 January 2019

Keywords:
Osteoarthritis
Opioids
Pain
Analgesics
Epidemiology
Pharmacology

SUMMARY

Objective: To quantify opioid use in knee and hip osteoarthritis (OA) patients, and to estimate the proportion of opioids in the population attributable to OA patients.
Design: Population-based cohort study.
Methods: We included 751,579 residents in southern Sweden, aged ≥35 years in 2015. Doctor-diagnosed knee or hip OA between 1998 and 2015 was the exposure. Dispensed weak and strong opioids were identified between November 2013 and October 2015 from the Swedish Prescribed Drug Register (SPDR). We determined age- and sex-standardized 12-month period prevalence of opioid use from November 2014 until October 2015 and calculated prevalence ratios and incidence rate ratios adjusted for age, sex, and other socio-demographic variables. We estimated the population attributable fraction (PAF) of incident opioid use attributable to OA patients.
Results: The 12-month prevalence of opioid use among OA patients was 23.7% [95% confidence intervals (CI) 23.3–24.2], which was two-fold higher compared to individuals without knee or hip OA: prevalence ratio: 2.1 [95% CI 2.1–2.1]. Similarly, OA patients were more likely to have an incident opioid dispensation, especially for strong opioids (incidence rate ratio: 2.6 [95% CI 2.5–2.7]). Population attributable tractions (PAF) of incident opioid use attributable to OA patients was 12%, 9% for weak and 17% for strong opioids.
Conclusions: Every fourth patient with knee or hip OA has opioids dispensed over a 1-year period, and 12% of incident opioid dispensations are attributable to OA and/or its related comorbidities. These results highlight that patients with knee and hip OA constitute a group of patients with an alarmingly high use of opioids.

Introduction

Chronic pain affects 20–30% of the adult population in western countries, with musculoskeletal disorders being the most common cause[1,2]. Opioids have been reported to be increasingly used to treat chronic pain conditions, including pain caused by musculoskeletal disorders[3,4], and sales of opioids in the US have been reported to have quadrupled from 1999 to 2010[5]. Further, it has been estimated that patients with *non-cancer* chronic pain conditions account for more than 2/3 of the total opioid consumption[6]. Opioids are potent analgesic pharmaceuticals but often have side effects such as nausea, constipation, and somnolence, and usage is associated with a high risk of addiction[7–9]. For older people using opioids to treat chronic pain conditions the risk of side effects is further amplified by coexisting co-morbidities and risk of drug–drug interactions[10]. Similarly, the risk of falls is also increased when using medications acting on the central nervous system such as opioids in older people[11,12] including for patients with osteoarthritis (OA)[13].

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https://doi.org/10.1016/j.joca.2019.01.005

OA is one of the major and steadily growing chronic musculoskeletal pain conditions in the middle-aged and elderly population[2], with more than 250 million people world-wide suffering from knee OA alone according to the Global Burden of Disease Study[14]. International clinical guidelines are reluctant with recommending opioids for patients with knee and hip OA as the risk-benefit of opioid use is uncertain[15,16]. End-stage treatment for patients with knee or hip OA is total joint replacement. Similar to other major surgical procedures about 7% of patients undergoing total knee or hip joint replacement show persistent use of opioids in the year following their surgery, potentially amplifying the risk of addiction[17,18]. Both long-term preoperative and postoperative opioid use after knee and hip replacement surgery, respectively, has been reported to be associated with increased risk of revision surgery[19,20].

Even though several warning flags have been raised in the literature concerning opioid use by OA patients[21–23], much uncertainty remains. For instance, there is great paucity of data describing opioid use in OA patients, especially in the context of *overall* opioid use in comparison to the general population, and the proportion of total opioid prescriptions that are attributable to OA is largely unknown. Such information is important for understanding the utilization of opioids in a large group of chronic pain patients.

Thus, the aims of our study were: *i)* to estimate the point prevalence and annual period prevalence as well as the incidence rate of dispensed weak *and* strong opioid in patients with and without knee and hip OA, using data from an entire geographically well-defined population in southern Sweden; *ii)* to estimate the proportion of dispensed weak and strong opioids in the general population $\geq$35 years attributable to knee and/or hip OA (or its related comorbidities).

Methods

Data sources

In Sweden, healthcare is provided from both public and private healthcare providers through the same tax-based financing system. All Swedish residents have a personal identification number, which includes information on age and sex. Swedish law requires all healthcare providers to submit information about healthcare contacts for reimbursement purposes. In the southernmost region of Sweden, covering about one-eighth of the Swedish population, all healthcare visits (both public and private) are registered within the Skåne Healthcare Register (SHR)[24]. The data is stored using each individual's unique personal identification number and contact date. Furthermore, the register contains the publicly practicing physicians' diagnostic codes according to the International Classification of Diseases (ICD) 10 system. The physicians themselves assign these codes, which are retrieved from the electronic medical records into the SHR.

Information about all *dispensed* opioid prescriptions on an individual basis is available via the Swedish Prescribed Drug Register (SPDR). Since July 2005 the SPDR has registered information on all dispensed prescriptions for all residents in Sweden, catalogued using the personal identification number. Individual level information on highest level of education reached, disposable income, marital status, and country of birth was retrieved from Statistics Sweden. The study was approved by the Lund University Ethical Review Committee (Dnr 2011-432 and 2014-276).

Prevalent knee and hip OA

We defined persons with at least one diagnostic code for knee OA (ICD-10 code: M17) or hip OA (M16) in the period between Jan 1^{s} 1998 and Oct 31st 2015 as having prevalent knee or hip OA. Participants with no record/s of either knee or hip OA diagnosis in the same period were defined as *not exposed* to knee or hip OA. Persons with *both* diagnoses were classified as having *both* knee and hip OA.

Prevalent and incident opioid use

We identified all dispensed opioid prescriptions through SPDR between Nov 1st 2013 and Oct 31st 2015 using Anatomical Therapeutic Chemical (ATC) codes from group N02A. We classified opioids as either 'weak' (i.e., Codeine and Tramadol) or 'strong' (i.e., Morphine, Oxycodone (incl. combinations), Fentanyl, Buprenorphine, Ketobemidone, Tapentadol, Hydromorphone, Pentazocine and Pethidine) as described in the 'Recommendations for the appropriate use of opioids for persistent non-cancer pain'[25]. If a person had an active prescription of both weak and strong opioids prescribed at the same time, we included this person in calculations related to both types of opioids. However, in calculations of *any* dispensed opioid, this person was included only once.

For the estimation of dispensed opioid *point prevalence* on Oct 4th 2015, a person contributed to the numerator when this day was included in the interval between the dispensing date and the theoretical end date of the prescription. The theoretical end date of the prescription was calculated as the dispensing date plus the prescribed duration of use (the number of total daily doses dispensed). For the estimation of the 12-month *period prevalence* (Nov 1st 2014 to Oct 31st 2015), all persons with a dispensed opioid within this time period were included in the numerator.

Dispensed opioid *incidence rates* were estimated among persons without any dispensed opioid during 1 year preceding the start of the follow-up period (i.e., without a dispensed opioid between Nov 1st 2013 and Oct 31st 2014). We calculated the time from Nov 1st 2014 to the first dispensed opioid or Oct 31st 2015, whichever came first.

Statistics

Descriptive statistics are reported as means and standard deviations (SD) or numbers with percentages as appropriate. Dispensed opioid point prevalence (on Oct 4th 2015) and 12-month period prevalence (Nov 1st 2014 to Oct 31st 2015) are reported as percentages with 95% confidence intervals (CI), crude as well as age- and sex-standardized to the Skåne population in the year 2015. Dispensed opioid incidence rates are presented per 1000 person-years with 95% CI, crude and age- and sex-standardized to the Skåne population at risk for opioid use. The 95% CIs for the crude proportions were calculated using the Agresti-Coull method and for crude incidence rates as mean of Poisson distribution, taking the time at risk into account. The 95% CIs for standardized proportions and rates were calculated using the function *dstdize* in Stata[26]. As recent surgery is associated with opioid use for postoperative pain, we also report incidence rates *excluding* any dispensed opioids 0–30 days *after* a surgical procedure, calculated from the discharge date and performed a sensitivity analysis to assess the impact of OA on opioid use that is not directly related to surgical treatment. Dispensed opioid prevalence ratios and incidence rate ratios were estimated using Poisson regression models with robust standard errors. Models were adjusted for age, sex, income category, highest education level reached, residential area, civil status and country of birth (Sweden vs others). Finally, we calculated the population attributable fractions (PAF) of dispensed opioid *incidence rates* derived from the Poisson models, by calculating ratio of conditional predicted incidence rates with 95%CI in a true observed scenario as in our data compared to a hypothetical scenario where no one

Table I
Description of the study sample, Skåne residents in the year 2015 aged 35 or older, $n = 751,579$

	No OA ($n = 669,200$)	Knee *and/or* hip OA ($n = 82,379$)	Knee OA ($n = 53,290$)	Hip OA ($n = 19,824$)	Knee *and* Hip OA ($n = 9265$)
Age, years, mean (SD)	56.3 (14.4)	70.3 (12.4)	68.6 (12.5)	72.4 (12.0)	75.7 (10.3)
Men, *n* (%)	332,649 (50)	34,934 (42)	22,850 (43)	8610 (43)	3474 (37)
Income, 100,000 SEK, mean (SD)*	2.51 (4.35)	2.18 (2.42)	2.22 (2.34)	2.19 (2.83)	1.94 (1.77)
Education:					
up to 9 years, *n* (%)	129,150 (20)	27,061 (33)	16,822 (32)	6621 (34)	3618 (40)
10–12 years, *n* (%)	275,800 (43)	34,622 (43)	22,923 (44)	8010 (41)	3689 (40)
13–14 years, *n* (%)	86,481 (13)	8549 (11)	5646 (11)	2053 (10)	850 (9)
15 + years, *n* (%)	151,115 (24)	10,918 (13)	7038 (13)	2882 (15)	998 (11)
Married, *n* (%)	459,844 (70)	59,385 (72)	39,182 (74)	13,888 (70)	6315 (68)
Born outside Sweden, *n* (%)	152,187 (23)	12,468 (15)	8858 (17)	2449 (12)	1161 (13)
Resident in Malmö†	154,581 (23)	14,789 (18)	10,014 (19)	3283 (17)	1492 (16)

OA=Osteoarthritis.
* SEK converted into 100,000 Euro (€) using the average 2015 exchange rate: No OA = 0.27€; Knee and/or hip OA = 0.23€; Knee OA = 0.24€; Hip OA = 0.23€; Knee and hip OA = 0.21€.
† Malmö is the largest (and only) metropolitan area within Skåne.

would have OA[27]. For this we used the function *punaf* in Stata[28]. Stata MP 15.1 was used for all analyses.

Results

There were 751,579 residents aged 35 years or older in Skåne, Sweden during 2015. Of those, 82,379 (11%) had prevalent knee and/or hip OA, 53,290 (7%) had prevalent knee OA only, 19,824 (3%) had prevalent hip OA only, and 9265 (1%) had both prevalent knee and hip OA. In general, more women than men had prevalent knee or hip OA, and individuals with OA were older than those without OA (Table I).

The 12-month period prevalence of any dispensed opioid among individuals with knee and/or hip OA was 23.6% (95% CI 23.3, 24.2) compared with 9.6% (95% CI 9.6, 9,7) among those without knee or hip OA, corresponding to a 12-month prevalence ratio of 2.1 (95% CI 2.1, 2.1) (Table II). Point prevalence estimates showed that 4.6% (95% CI 4.4, 4.9) of patients with knee and/or hip OA had an active dispensed prescription of an opioid on Oct 4th 2015. Similarly, dispensing incidence rates (i.e., new opioid use) of any opioid among those without dispensed opioids in the preceding year were 2.3-fold higher (95% CI 2.3, 2.4) among those with knee and/or hip OA compared to those without (Table III). Our data showed that 11.8% (95% CI 11.3, 12.3) of any new (i.e., incident) opioid prescription dispensed were to a patient with knee and/or hip OA (i.e., population attributable fraction (PAF)).

In general, 12-month period prevalence ratios and incidence rate ratios for dispensing of weak opioids were similar between patients with either knee or hip OA, but somewhat higher among those with combined knee and hip OA (Tables II and III). However, prevalence ratios and incidence rate ratios for dispensing of strong opioids were higher among patients with hip OA and patients with combined knee and hip OA than patients with knee OA alone (Tables II and III). The PAF of knee and/or hip OA for incident strong and weak opioids dispensed were 16.7% (95% CI 15.7, 17.6) and 9% (95% CI 8.4, 9.5), respectively. Age-stratified incidence rates showed that dispensing of weak opioids among patients with knee and/or hip OA decreased with increasing age, whereas the opposite pattern was observed for strong opioids (Figs. 1 and 2). Excluding opioid use within the 30 days following discharge after a surgical treatment attenuated the estimates of incidence rates for dispensed strong opioids markedly (Table III), although the incidence rate ratios remained essentially the same (Supplementary table 1).

Table II
Dispensed opioid 12-month period prevalence, point prevalence and prevalence ratio

	Crude, % (95% CI)	Standardized*, % (95% CI)	Adjusted prevalence ratio† (95% CI)
12-Month period prevalence			(Ref: no prevalent OA)
Any opioid			
No OA	9.3 (9.3, 9.4)	9.6 (9.6, 9.7)	–
Knee and/or hip OA	25.8 (25.5, 26.1)	23.7 (23.3, 24.2)	2.1 (2.1, 2.1)
Knee OA	23.4 (23.1, 23.8)	22.1 (21.5, 22.6)	2.0 (1.9, 2.0)
Hip OA	27.0 (26.4, 27.6)	25.9 (24.7, 27.1)	2.2 (2.1, 2.2)
Knee and Hip OA	36.8 (35.8, 37.8)	34.6 (30.9, 38.4)	2.7 (2.7, 4.0)
Weak opioids			
No OA	6.6 (6.6, 6.7)	6.7 (6.6, 6.8)	–
Knee and/or hip OA	15.1 (14.9, 15.4)	16.1 (15.7, 16.6)	2.0 (2.0, 2.1)
Knee OA	14.8 (14.5, 15,1)	15.8 (15.3, 16.3)	2.0 (1.9, 2.0)
Hip OA	14.2 (13.7, 14.7)	15.2 (14.2, 16.2)	1.9 (1.9, 2.0)
Knee and Hip OA	19.2 (18.4, 20.0)	23.0 (19.5, 26.5)	2.5 (2.4, 2.6)
Strong opioids			
No OA	3.7 (3.6, 3.7)	4.0 (3.9, 4.0)	–
Knee and/or hip OA	14.8 (14.5, 15.0)	11.5 (11.2, 11.8)	2.4 (2.4, 2.5)
Knee OA	12.2 (11.9, 12.5)	9.8 (9.4, 10.1)	2.1 (2.1, 2.2)
Hip OA	17.1 (16.5, 17.6)	14.7 (13.8, 15.6)	2.7 (2.6, 2.8)
Knee and Hip OA	24.7 (23.9, 25.6)	20.5 (17.5, 23.5)	3.4 (3.3, 3.6)
Point prevalence			(Ref: no prevalent OA)
Any opioid			
No OA	1.7 (1.7, 1.7)	1.7 (1.7, 1.8)	–
Knee and/or hip OA	4.7 (4.6, 4.9)	4.6 (4.4, 4.9)	2.1 (2.0, 2.2)
Knee OA	4.3 (4.1, 4.5)	4.3 (4.1, 4.6)	2.0 (1.9, 2.1)
Hip OA	4.7 (4.4, 5.0)	5.0 (4.4, 5.6)	2.1 (2.0, 2.3)
Knee and Hip OA	7.0 (6.5, 7.6)	5.7 (4.5, 6.8)	2.9 (2.6, 3.1)
Weak opioids			
No OA	1.3 (1.3, 1.4)	1.3 (1.3, 1.4)	–
Knee and/or hip OA	3.4 (3.3, 3.5)	3.7 (3.4, 3.9)	2.2 (2.1, 2.3)
Knee OA	3.2 (3.1, 3.4)	3.5 (3.2, 3.7)	2.1 (2.0, 2.2)
Hip OA	3.3 (3.0, 3.5)	3.7 (3.2, 4.3)	2.1 (1.9, 2.3)
Knee and Hip OA	4.7 (4.3, 5.1)	4.5 (3.4, 5.6)	2.8 (2.5, 3.1)
Strong opioids			
No OA	0.4 (0.4, 0.4)	0.4 (0.4, 0.4)	–
Knee and/or hip OA	1.4 (1.3, 1.5)	1.1 (1.0, 1.2)	2.1 (1.9, 2.2)
Knee OA	1.2 (1.1, 1.3)	1.0 (0.8, 1.1)	1.9 (1.7, 2.0)
Hip OA	1.5 (1.4, 1.7)	1.3 (1.0, 1.6)	2.1 (1.9, 2.4)
Knee and Hip OA	2.5 (2.2, 2.9)	1.4 (1.0, 1.8)	3.0 (2.6, 3.4)

OA=Osteoarthritis.
* Age- and sex-standardized to the Skåne population.
† Adjusted for age, sex, civil status, country of birth (Sweden vs others), income category, highest education level, residential area.

Table III
Incidence rates and incidence rate ratios of dispensed opioids (Nov 1st 2014 to Oct 31st 2015)

	Crude, per 1000 person years (95% CI)	Standardized*, per 1000 person years (95% CI)	Standardized† (excluding surgery opioid use), per 1000 person years (95% CI)	Adjusted incidence rate ratio‡ (95% CI) (Ref: no prevalent OA)
Any opioid				
No OA	50 (49, 50)	54 (53, 54)	47 (47, 48)	-
Knee and/or hip OA	148 (145, 151)	137 (132, 141)	112 (108, 116)	2.3 (2.3, 2.4)
Knee OA	131 (127, 134)	125 (120, 130)	105 (100, 110)	2.1 (2.0, 2.2)
Hip OA	165 (159, 172)	157 (146, 169)	121 (111, 132)	2.5 (2.4, 2.7)
Knee and Hip OA	226 (213, 238)	218 (177, 259)	174 (137, 212)	3.3 (3.1, 3.5)
Weak opioids				
No OA	31 (31, 32)	33 (32, 33)	31 (30, 31)	-
Knee and/or hip OA	68 (66, 70)	76 (72, 80)	69 (65, 72)	2.1 (2.0, 2.2)
Knee OA	66 (64, 69)	76 (72, 81)	67 (63, 71)	2.0 (1.9, 2.1)
Hip OA	64 (60, 69)	66 (58, 74)	64 (56, 72)	2.0 (1.9, 2.1)
Knee and Hip OA	87 (80, 95)	114 (78, 150)	106 (72, 141)	2.7 (2.5, 3.0)
Strong opioids				
No OA	19 (18, 19)	21 (21, 21)	17 (17, 17)	-
Knee and/or hip OA	81 (79, 83)	62 (59, 64)	45 (42, 47)	2.6 (2.5, 2.7)
Knee OA	65 (63, 68)	50 (47, 53)	38 (36, 41)	2.3 (2.2, 2.4)
Hip OA	102 (97, 107)	91 (83, 100)	58 (51, 65)	3.1 (2.9, 3.3)
Knee and Hip OA	140 (130, 150)	105 (82, 128)	69 (52, 86)	3.8 (3.5, 4.1)

OA=Osteoarthritis.
* Age- and sex-standardized to the Skåne population.
† Age- and sex-standardized to the Skåne population, excluding opioid use 0–30 days after surgical procedure discharge date.
‡ Adjusted for age, sex, civil status, country of birth (Sweden vs others), income category, highest education level, residential area.

The most common dispensed opioid among those with an incident opioid prescription was Codeine, which accounted for 43% of all incident dispensations, followed by Oxycodone (incl. combinations) (28%), Tramadol (16%) and Morphine (11%). However, the proportion of incident dispensations of weak vs strong opioids differed between individuals with knee and/or hip OA and those without. Among patients *with* knee and/or hip OA, strong opioids accounted for a higher proportion of total incident dispensations, particularly Oxycodone (38% vs 26%) and Morphine (14% vs 10%). Conversely, in individuals *without* OA, weak opioids accounted for a higher proportion of incident dispensations, such as Codeine (46% vs 33%) and Tramadol (17% vs 12%) (Supplementary table 2). This picture remained the same when excluding opioid use within 30 days after discharge from a surgical procedure (Supplementary table 3).

Discussion

About one in four southern Sweden residents with prevalent knee and/or hip OA have an opioid dispensation within a 1-year period. These proportions were considerably higher than in individuals *without* recorded knee or hip OA, of whom only about 10% had an opioid dispensed in the same period. Our results suggest that patients with knee and/or hip OA are therefore over 2 times

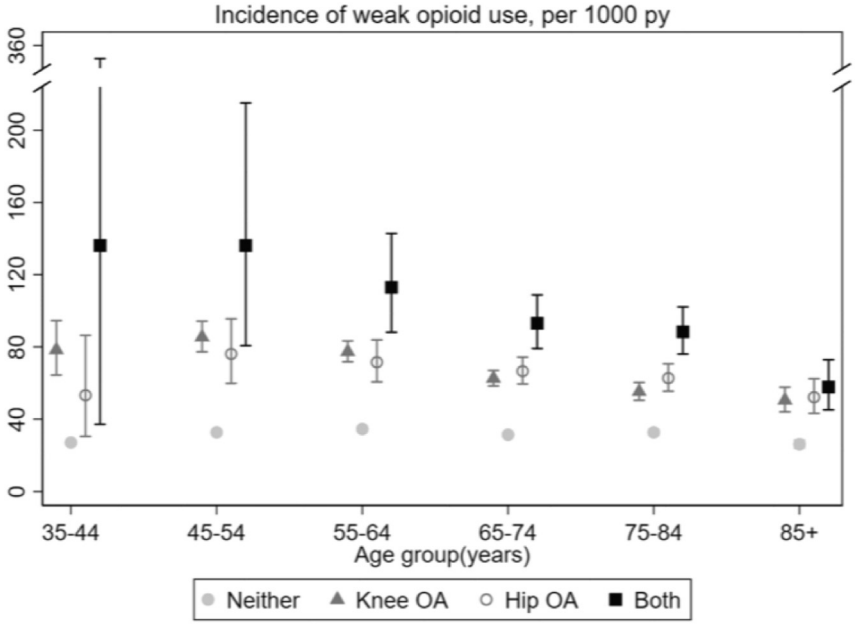

Fig. 1. Age-stratified incidence rates (95% confidence intervals (CI) for dispensing of *weak* opioids among individuals with prevalent knee and/or hip osteoarthritis compared with individuals without knee or hip osteoarthritis. The *y*-axis is broken to accommodate the high value of the upper confidence limit for the youngest age group.

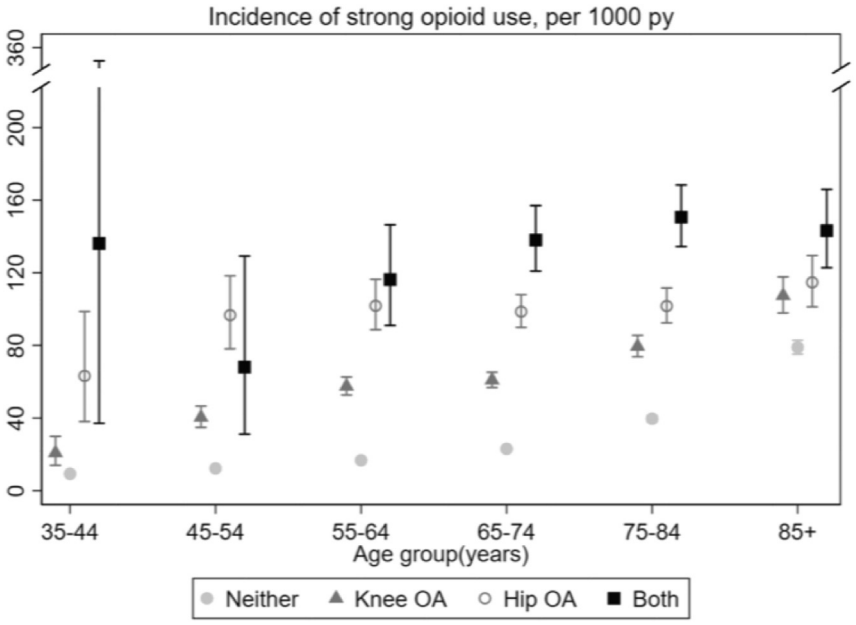

Fig. 2. Age-stratified incidence rates (95% CI) for dispensing of *strong* opioids among individuals with prevalent knee and/or hip osteoarthritis compares with individuals without knee or hip osteoarthritis. The *y*-axis is broken to accommodate the high value of the upper confidence limiet for the youngest age group.

more likely to have an opioid dispensed. Furthermore, patients with knee and/or hip OA were also twice as likely to start a new opioid prescription compared to individuals without OA. Finally, we report that 12% of new opioid use is attributable to knee and/or hip OA and/or their related comorbidities.

Use of opioids for chronic pain conditions has been reported to be increasing within recent years[4]. Some studies have reported on opioid use in patients with knee and hip OA[21–23,29], but in general, population-based estimates on current and new prescriptions for opioid use in individuals with knee and hip OA are still sparse. Our data suggest that 4–5% of individuals with doctor-diagnosed knee and/or hip OA have an active opioid prescription at any given time. Estimates were highest for the 1% of individuals having combined knee and hip OA. The likelihood of having a new opioid dispensed was also higher among individuals with knee and/or hip OA, compared to the population without knee or hip OA. This likelihood was higher for strong opioids, yielding an incidence rate ratio of 2.6 compared to 2.1 for weak opioids. Particularly, a much higher proportion of individuals with knee and/or hip OA had a new prescription for Oxycodone, compared to those without OA.

To the best of our knowledge, we are the first to report prevalence and incidence estimates of dispensed opioids among patients with prevalent knee and/or hip OA based on data from an entire population, and thus we have identified no data for direct comparison. It has previously been reported that the proportion of people with an opioid prescription has been stable in Sweden in the period from 2006 to 2015[30]. Nevertheless, our data still suggest that patients with knee and hip OA constitute a group of chronic pain patients with alarmingly high rates of opioid use, particularly since 9% and 17% of newly dispensed weak and strong opioids, respectively, can be attributed to knee and/or hip OA and their related comorbidities.

The high rates of opioid dispensing for patients with knee and/or hip OA is controversial given the reluctance of clinical guidelines for recommending opioids for OA patients due to risk of adverse events and addiction[15,16]. Paradoxically, first-line guideline recommended treatment such as exercise therapy[31,32], which is safe[33], shows similar or greater effect sizes than pharmacological treatments such as paracetamol, NSAIDs[34] and opioids[35,36] in comparison with control interventions or placebo for reducing knee and hip OA pain. However, quality of care studies report that exercise therapy is heavily underutilized[37,38], and it may be speculated that the perception of strong pain medication as an 'easy and quick fix' solution may present a barrier for utilization of more safe and effective treatments. Adding to this, opioid use has been associated with increased healthcare utilization and cost, especially among individuals with long-term use[39].

Surgeries such as knee arthroscopy and joint replacements are common among patients with knee or hip OA, and time-limited postoperative use of opioids is often standard. However, more than 7% of patients undergoing total hip or knee joint replacement show persistent use of opioids, in the year following joint replacement, which can lead to addiction[17]. In sensitivity analyses we sought to take recent surgery into account by excluding opioid use within the first 30 days from discharge after a surgical procedure. As expected, incidence rates of dispensed strong opioids were substantially lowered. However, incidence rate ratios between individuals with knee and/or hip OA and the population without OA were only marginally attenuated, suggesting that opioid use is elevated in persons with OA not undergoing surgery or can persist long after surgical intervention.

Certain important considerations should be made in interpreting this study. One limitation is that we defined prevalent knee and hip OA up until Oct 31st 2015, the latest time point available in our dataset. This definition would include a small number of cases of opioid use prior to OA diagnosis as being OA-related when assessing the 12-month prevalence (in the period Nov 1st to Oct 31st 2015). However, OA is a slowly developing disease, often taking years to develop. Therefore, we assume that opioid use close to OA diagnosis is still likely to be disease-related. Misclassification of disease is also always a source of concern in such register-based studies. However, the validity of the doctors' diagnostic coding in the SHR has been reported to be high[40]. Further, in Sweden only 2 of 3 persons with symptomatic knee OA consult healthcare[41], and we were not able to assess opioid use in those who did not consult a physician. However, opioids can only legally be prescribed by physicians.

Based on the current data, it was not possible to determine what condition the prescribed opioids were prescribed for as no diagnosis was available as part of the dispensing data. We chose not to adjust our analysis for the presence of other diagnosis, which may be related to opioid use because it is not known if these co-morbidities precede or follow as a consequence of knee and/or hip OA.

As with all studies using data on dispensed drugs, we do not know what percentage of all prescribed opioids were dispensed, and the patient compliance in relation to dispensed drugs.

Finally, we performed sensitivity analyses assessing point prevalence of opioid use on the 4th of January, April and July (data not shown), which provided similar estimates to those for Oct 4th, presented in this study. This suggests negligible effects of the choice of day on the point prevalence assessment.

In conclusion, we found that approximately one in every four individuals with knee and/or hip OA had opioids dispensed within a 12-month period, which was more than twice as many as among the population without knee or hip OA. Similarly, individuals with knee and/or hip OA were more than twice as likely to have a new (incident) dispensation of an opioid compared to those without OA. Recent surgery accounted for a considerable proportion of strong opioid use, however incidence rate ratios between individuals with and without knee and/or hip OA was only marginally affected when taking this into account. Of the incident opioid dispensations in individuals aged 35 years or older, 9% of weak and 17% of strong opioids, respectively, could be attributed to knee and/or hip OA and/or their related comorbidities. These results highlight that patients with knee and hip OA are an important group of patients having an alarmingly high use of prescription opioids. Findings call for increased awareness and better utilization of other core OA treatments, as well as point to a general need for better management of OA as a growing public health concern.

Contributions

ME and AT conceived the study. JBT, AT and ME designed the study, and AT performed the statistical analysis. All authors participated in interpretation of the data. JBT drafted the manuscript, which was revised and edited by all co-authors for important intellectual content. All authors approved the final version of the manuscript to be published.

Competing interests

Dr. Prieto-Alhambra reports grants and other from Amgen, grants and other from UCB Biopharma SPRL, outside the submitted work. Dr. Englund reports grants from The Swedish Research Council, grants from Österlund Foundation, grants from Governmental Funding of Clinical Research within National Health Service (ALF), grants from Greta and Johan Kock Foundation, grants from The Swedish Rheumatism Association, during the conduct of the study. The remaining authors declare no conflict of interest.

Role of the funding sources

This work was supported by funds from The Swedish Research Council, Österlund Foundation, Governmental Funding of Clinical Research within National Health Service (ALF), Greta and Johan Kock Foundation, and The Swedish Rheumatism Association. None of the funding sources were involved in any part of the study or about the decision to submit the manuscript for publication.

Acknowledgements

We would like to acknowledge Velocity Hughes, PhD, for her contribution to the manuscript with language editing.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2019.01.005.

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